EPID600 (Spring 2007) module on Information Bias

Objectives:

- Differentiate information bias from selection bias.
- List the major sources of information bias in given epidemiologic studies.
- Distinguish between differential and non-differential misclassification bias.
- Explain the effect that non-differential misclassification bias can have on the measures of association in a given study.
- Explain the effect that differential information bias can have on the measures of association in a given study.
- Describe how information bias can be reduced or eliminated in epidemiologic studies.
- Identify methods to measure exposure.
- Identify and evaluate the potential for information bias associated with the investigator's method of assessing exposures in epidemiologic studies.
- Discuss interviewer bias.
- Explain how training of interviewers can minimize interviewer bias.
- Recognize differential and nondifferential misclassification bias in an actual study.
- Based on a 2x2 table you have constructed, quantify the effect of non-differential misclassification on the odds ratio (OR).

Instructions:

1. **Read**: Aschengrau and Seage, ch. 10 - Bias . Answer the practice questions at the end of the chapter or at http://publichealth.jbpub.com/aschengrau/student_resources.cfm and check your answers (recommended, but optional) (animated flashcards, weblinks, and Powerpoint slides from the authors] can also be found at that URL)

2. Look over the case study questions and then read the case study reading: Gelberg et al. (1995). Fluoride exposure and childhood osteosarcoma: a case-control study. *Am J Public Health* 85(12), 1678-1683. (abstract, **UNC-CH**: full text)

3. (Optional, but earns credit) Before lab, submit the answers to the starred case study questions (numbers 3, 4, 5, 7, and 10).

4. Read the lecture slides and attend the lecture (or read the speaker notes).

5. Work on the rest of the case study questions in **lab** and afterwards.

6. Agree on the answers, so the facilitator can submit the group's consensus answers by the following Sunday evening (EST).

Case Study Questions (NOTE: For some of these questions there may not be one "right answer".)

1. Name the sources that were used to determine the cumulative lifetime exposure to fluoride.

2. How was exposure to fluoride in drinking water measured?

**3. Is it possible that this method of ascertaining exposure could lead to a type of information bias? If so, do you think it would be differential or nondifferential misclassification bias?

a. How was exposure to ingested fluoride measured?

b. Could this method of measurement lead to a type of information bias? Why or why not? Do you think it would be differential or non-differential?

**4. Do you think it is likely that subjects were misclassified in regard to their disease status? Explain.

**5. On page 1680 of the article, the authors state that "the cumulative lifetime exposure for each fluoride source was estimated in milligrams by multiplying the amount ingested per exposure by the number of times per day exposed by the total number of days exposed. The lifetime exposures for each fluoride source were then summed to create a total lifetime fluoride exposure index."

How accurate do you think this exposure index would be? Could a bias have been introduced by the use of this index? If so, what effect would this bias have had on the authors' estimate of the association between fluoride and osteosarcoma (i.e. would the bias be differential or non-differential and how would that effect the study's results)?

6. Does the potential for interviewer bias occur in this study? Explain.

**7. List some things that the investigators might have done differently in conducting this study that would have eliminated the possibility of the types of information bias you've already described.

[continues on next page]

Quantitative Assessment of Information Bias

The following 2 x 2 table is derived from Table 1 of the Gelberg article. Exposure to fluoride from drinking water was derived by combining USDA data of population-based estimates of water consumption and estimated fluoride levels for each subject's residential water supply.

Fluoride exp. in water	Cases	Controls	Total
1851-6100 mg	50 (=a)	49 (=b)	99
0 mg	40 (=c)	57 (=d)	97
Total	90	106	196

8. Calculate the observed odds ratio for cases of osteosarcoma versus controls.

9. Suppose that this study's method of classifying exposure underestimated fluoride consumption and that this misclassification was nondifferential. Assume that the sensitivity of the survey was 80%. That is, only 80% of the individuals exposed to 1851-6100 mg of fluoridated water were categorized that way (True Positives) and the other 20% were incorrectly categorized as unexposed (False Negatives).

Using all of the given information, construct the corrected 2 x 2 table which shows the true fluoride exposure for cases and controls. (Internet course: You do not need to submit the table to your TA.)

HINT:
Let: A=true number of exposed cases; a=observed number (80% of A)
B=true number of exposed controls; b=observed number (80% of B)
C=true number of unexposed cases; c=observed number
D=true number of unexposed controls; d=observed number

10. Calculate the corrected OR for osteosarcoma associated with fluoride and compare this new 'true' OR to the 'observed' OR. What was the effect of the non-differential misclassification on the observed odds ratio? In which direction did the misclassification bias the OR?

12/10/2001vs/lka, 3/24/2004vs, 7/21/2005vs

Fluoride Exposure and Childhood Osteosarcoma: A Case–Control Study

Kitty H. Gelberg, PhD, MPH, Edward F. Fitzgerald, PhD, Syni-an Hwang, PhD, and Robert Dubrow, MD, PhD

ABSTRACT

Objectives. This study tests the hypothesis that fluoride exposure in a nonoccupational setting is a risk factor for childhood osteosarcoma.

Methods. A population-based case–control study was conducted among residents of New York State, excluding New York City. Case subjects (n = 130) were diagnosed with osteosarcoma between 1978 and 1988, at age 24 years or younger. Control subjects were matched to case subjects on year of birth and sex. Exposure information was obtained by a telephone interview with the subject, parent, or both.

Results. Based on the parents' responses, total lifetime fluoride exposure was not significantly associated with osteosarcoma among all subjects combined or among females. However, a significant protective trend was observed among males. Protective trends were observed for fluoridated toothpaste, fluoride tablets, and dental fluoride treatments among all subjects and among males. Based on the subjects' responses, no significant associations between fluoride exposure and osteosarcoma were observed.

Conclusions. Fluoride exposure does not increase the risk of osteosarcoma and may be protective in males. The protective effect may not be directly due to fluoride exposure but to other factors associated with good dental hygiene. There is also biologic plausibility for a protective effect. (*Am J Public Health.* 1995;85:1678–1683)

Introduction

Although the benefit to dental health of fluoride exposure has been clearly established, the release of the National Toxicology Program study in which a dose–response relationship for osteosarcoma was indicated for exposure to sodium fluoride among male rats has provoked criticism of water fluoridation programs.[1] In response, the Department of Health and Human Services conducted a review of fluoride's benefits and risks and recommended that analytical epidemiologic studies of osteosarcoma be conducted to determine the risk factors associated with its development.[2]

Osteosarcoma is the fourth most common cancer in persons under 25 years of age[3] occurring most often around puberty.[4] The only known etiological agent is radiation[5]; other suggested risk factors include a rapid rate of bone growth, previous bone trauma, and viruses.[6–8] Persons with the hereditary form of retinoblastoma or with the Li–Fraumeni cancer family syndrome are at high risk for osteosarcoma.[9,10]

Fluoride is deposited directly into the bone, with about 99% of fluoride in the body contained in the skeleton.[1,2] Children, who are actively forming bone, have a higher amount of uptake of fluoride into the bone matrix than adults.[1,2] Fluoride uptake into bone results in an increased rate of osteoblast proliferation and bone formation.[11] Bone in the areas of the knees, ankles, shoulders, and wrists, where childhood osteosarcomas most often occur, shows a high response to fluoride.[12]

Toxicological studies of sodium fluoride have yielded mixed results.[1,13–15] In in vitro studies fluoride appears to be mutagenic and can induce chromosome aberrations, sister chromatid exchanges, cytotoxicity, and neoplastic transformation in cultured mammalian cells.[1,13,14] The recent study conducted by the National Toxicology Program found equivocal evidence for a carcinogenic effect among male F344/N rats, but there was no evidence for carcinogenicity in female F344/N rats, nor in male or female mice.[1] Another study sponsored by the Procter and Gamble company found no carcinogenic evidence in Sprague–Dawley rats.[16]

Ecological studies generally have found no relationship between fluoride levels in drinking water and osteosarcoma and bone cancer incidence or mortality rates.[17–23] Individual exposures were examined in only two small studies.[24,25] One study based on only 20 males found that males under age 20 years who resided in communities with fluoridated water at the time of diagnosis had a higher osteosarcoma rate than those who resided in communities with nonfluoridated water.[24] The other study had only 22 matched case–control pairs and found no associa-

Kitty H. Gelberg is with the Bureau of Occupational Health, New York State Department of Health, Albany, NY, and the Department of Epidemiology and Public Health, Yale University School of Medicine, New Haven, Conn. Edward F. Fitzgerald and Syni-an Hwang are with the Bureau of Environmental and Occupational Epidemiology, New York State Department of Health. Robert Dubrow is with the Department of Epidemiology and Public Health, Yale University School of Medicine.

Requests for reprints should be sent to Kitty H. Gelberg, PhD, MPH, New York State Department of Health, 2 University Place, Rm 155, Albany, NY 12203.

This paper was accepted July 31, 1995.

Note. The views expressed here are the authors' and do not necessarily represent those of the National Cancer Institute.

Principles of Epidemiology for Public Health (EPID600)

Sources of error: Information bias

Victor J. Schoenbach, PhD home page

Department of Epidemiology
School of Public Health
University of North Carolina at Chapel Hill

www.unc.edu/epid600/

Chapter 1
THE HISTORIAN'S TASK:
Insight into the future

History, a record of things left behind by past generations, started in 1815. Thus we should try to view historical times as the behind of the present.

Anders Henriiksson (ed), *Non Campus Mentis*, NY, Workman Publishing Co., 2003

Non Campus Mentis

"History, as we know, is always bias, because human beings have to be studied by other human beings, not by independent observers of another species."

Anders Henriiksson (ed), *Non Campus Mentis*, NY, Workman Publishing Co., 2003, chapter 1

Abort, Retry, Fail

"Tips for safer drives: Never turn off a PC or accessories while the computer is on or the disk is active."

— *USA Today*

[*PC Magazine*, 10/3/1996]

Information bias can arise from misunderstanding the interviewer

- Medico – Não consigo encontrar o motivo das suas dores, meu caro. Só pode ser por causa da bebida.
- Paciente – Não tem importãncia, doutor. Eu volto outro dia que o senhor estiver sóbrio.

De Luciana V. Paiva, Osasco - SP, en Bom Humor Nosso E Dos Leitores", *Almanaque Brasil de Cultura Popular*. Maio 2001;3(26) (almanaquebrasil@uol.com.br). Exemplar de quem viaja TAM.

Selection bias in the news

- Classic experiment by Yale psychologist Stanley Milgram
- Asked people in Kansas to forward a letter to a target person in Massachusetts
- If did not know target person, then send it to someone they thought might know him
- His 1967 paper reported that it only took 5 jumps, on average, for letters to arrive

Selection bias in the news

According to Judith Kleinfeld, psychologist at the University of Alaska, Fairbanks, archives reveal that only 30% of the letters actually reached their destination! [*Society*, in press]

(Gewolb, Josh. Random samples. *Science* 26 October 2001;294:777)

Dr. Kinsey and the Institute for Sex Research

Alfred S. Kinsey (photograph from Wardell B. Pomeroy, *Dr. Kinsey and the Institute for Sex Research*)

Sex research in the mid-20th century

Alfred S. Kinsey (photograph from Wardell B. Pomeroy, *Dr. Kinsey and the Institute for Sex Research*)

Sex survey, circa 1926

North Carolina sex survey published in 1926:

"Has anyone ever tried to give you the mistaken idea that sex intercourse is necessary for the health of the young man?"

(Alfred C. Kinsey, Wardell B. Pomeroy, Clyde E. Martin. *Sexual behavior in the human male*, Phila, W.B. Saunders, 1948)

Kinsey *et al*. on selection and information bias

Alfred S. Kinsey (photograph from Wardell B. Pomeroy, *Dr. Kinsey and the Institute for Sex Research*)

Information bias

- Classification or measurement
- Differential or nondifferential
- Direction of bias
- Misclassification of a third variable
- Independence of errors

Classification or measurement

- Data for epidemiologic studies consist of classifications (e.g., "case"/"non-case") or measurements (e.g., 120 mmHg systolic BP).
- Possible sources of measurement or classification error include respondents, data collectors, data managers, data analysts, data interpreters.

Sources of measurement error

- Respondent: inability to understand, recall, articulate; unwillingness to disclose or social desirability
- Data collector: unclear or ambiguous questions, lack of a neutral demeanor, insufficiently conscientious, inaccurate transcription, fraud

Sources of measurement error

- Data managers: inaccurate transcription, mis-reading, miscoding, programming errors
- Data analysts: variable coding and programming errors
- Data interpreters: inadequate appreciation of the characteristics of the measure or of the relations being studied

The War on Error

- Precise operational definitions of variables
- Detailed measurement protocols
- Repeated measurements on key variables
- Training, certification, and re-certification
- Data audits (of interviewers, of data centers)
- Data cleaning – visual, computer
- Re-running all analyses prior to publication

Information bias – differential or non-differential

- Important question for any kind of bias – are error processes different for groups being compared
  - If no, "non-differential"
  - If yes, "differential"
- Has implications for direction of bias
- In general, non-differential is safer

Direction of bias

- "Upward"
- "Downward"
- "Towards the null"
- "Away from the null"

Direction of bias

In simple situation, information bias is towards the null IF:

1. Dichotomous exposure and disease
2. Non-differential misclassification with both sensitivity and specificity each greater than 0.5; AND
3. Errors in one variable are independent of errors in the other

Errors in covariables

- It is almost always important to control for other variables (e.g., age)
- Errors in measurement of these variables hamper attempts to control for them
- Direction of bias is generally unpredictable

Real-life example: *Quit for Life*

- Randomized trial of smoking cessation interventions
- Self-reported "In the past 7 days, have you smoked a cigarette, even a puff?"
- Attempted (unsuccessfully) to validate with saliva cotinine
- People unwilling to schedule an appointment had very high quit rates!

Kinsey biography by Wardell Pomeroy


Staff conference, 1953. Left to right: Kinsey, Martin, Gebhard and Pomeroy. *Dellenback*

Pomeroy, Wardell B. *Dr. Kinsey and the Institute for Sex Research* NY, Signet / New American Library, 1972: p136

Non Campus Mentis

"Hindsight, after all, is caused by a lack of foresight."

Anders Henriiksson (ed), *Non Campus Mentis*, NY, Workman Publishing Co., 2003, chapter 1